Cost effectiveness of EUS for preoperative localization of pancreatic endocrine tumours
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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Endoscopic ultrasonography (EUS) for early preoperative localisation of pancreatic neuroendocrine tumours. A set of EUS-based protocols was adopted in the study, based on the idea of using pancreatic angiography and arterial stimulation and venous sampling (ASVS) only when EUS did not help to localise the tumour. Different EUS-based protocols were applied for groups of patients: Patients with sporadic insulinoma received EUS first followed by surgical exploration if a tumour is detected. CT is performed to exclude metastatic disease if a locally invasive tumour or one larger than 3cm is seen. ASVS with intra-arterial calcium simulation is performed before exploration in cases where EUS does not help identify a tumour; Patients with sporadic gastrinoma received EUS after metastatic disease has been excluded by CT. ASVS with intra-arterial secretin stimulation (Imamura test) is optional; Patients with multiple endocrine neoplasia (MEN) type I receive abdominal CT and EUS.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with pancreatic neuroendocrine tumours.

Setting
Hospital. The economic analysis was carried out in Michigan, USA.

Dates to which data relate
Effectiveness and resource use data corresponded to patients examined in the study institution during the period between February 1993 and January 1996 for the EUS group and the 5-year period before the introduction of EUS for pre-EUS group. The price year was 1995.

Source of effectiveness data
The evidence for the final outcomes was based on a single study.

Link between effectiveness and cost data
Costing was conducted retrospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not used to determine the sample size. The study sample consisted of 36 patients with a mean
(SD) age of 46 (2.4) years who underwent preoperative EUS (EUS group). They were matched retrospectively with 36 patients with a mean (SD) age of 46.8 (2.3) years who were examined in the 5-year period before the introduction of EUS (pre-EUS group). 8 patients examined with EUS were excluded because researchers were unable to find an appropriately matched patient from the pre-EUS cohort.

**Study design**
This was a retrospective cohort study, carried out in a single centre. The mean duration of follow-up appears to have been until discharge from hospital. No information was provided regarding the number of patients who were lost to follow-up. Tumour size, echotexture, location within the pancreas, involvement of the peripancreatic vessels, and the presence of regional lymph nodes were documented and compared with surgical findings. The medical records of all patients were reviewed.

**Analysis of effectiveness**
Patients were analysed in the groups to which they belonged. The effectiveness measure was the confirmation of the presence and location of a pancreatic neuroendocrine tumour as defined in the preoperative imaging strategy by the findings at surgical exploration and surgical pathologic findings. The patient groups were matched in terms of age, sex, and tumour type.

**Effectiveness results**
A neuroendocrine tumour was accurately localised by means of preoperative imaging for 31 of the patients in the pre-EUS group (86% accuracy) and 30 of the patients in the EUS group (83% accuracy), (not significant). In the EUS group, 4 patients had tumours in the head of the pancreas undetected with all imaging tests, and 2 patients had normal results of imaging studies and no tumour found at surgical exploration. In the pre-EUS group, 1 duodenal tumour and 1 tumour in the tail of the pancreas were detected with ASVS procedures, and 3 patients had no tumour at laparotomy despite abnormal findings at ASVS. It was reported that EUS allowed accurate prediction of the presence or absence of a surgically detectable pancreatic tumour for all 8 patients who were excluded from the EUS group.

**Clinical conclusions**
The authors emphasised EUS at the time of the study because in their experience this technique has been 100% sensitive in the identification of pancreatic primary gastrinoma. The presence of normal findings at EUS of the pancreas is a reliable predictor of extrapancreatic gastrinoma, invariably located in the duodenum. Duodenotomy is always indicated for this group of patients.

**Measure of benefits used in the economic analysis**
The measure of benefit was the number of accurately localised tumours.

**Direct costs**
Costs were not discounted due to the short time frame of the cost analysis. Quantities were reported separately from the costs and some of the cost items were reported separately. The cost analysis covered the costs of diagnostic procedures: procedural charges and hospital admissions specifically required for preoperative localisation. The boundary in the cost analysis was not explicitly specified but appears to have been the hospital. Charges, in terms of hospital and professional fees, were obtained from the study institution and were used as a proxy for true costs. The cost of angiography and selective venous blood sampling was underestimated because the charges for serial hormone assays were not included. The cost of procedure-related morbidity was not included in the cost analysis. The price year was 1995.

**Statistical analysis of costs**
Student’s t test was used to compare the groups in terms of costs.
Indirect Costs
Indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
A neuroendocrine tumour was accurately localised by means of preoperative imaging for 31 of the patients in the pre-EUS group (86% accuracy) and 30 of the patients in the EUS group (83% accuracy), (not significant).

Cost results
The total charge per patient was $4,846 in the pre-EUS group and $2,620 in the EUS group, (p<0.05).

Synthesis of costs and benefits
The cost-effectiveness measure was the cost of imaging procedures per accurately localised tumour, which amounted to $3,144 for the EUS group and $5,628 for the pre-EUS group, (p<0.05). No incremental analysis was performed as EUS was the weakly dominant strategy.

Authors’ conclusions
EUS is highly accurate in the localisation of pancreatic neuroendocrine tumours and is cost-effective when used early in the preoperative localisation strategy. EUS decreased the need for additional invasive tests and avoided unnecessary morbidity and resource consumption.

CRD COMMENTARY - Selection of comparators
The strategy of using conventional imaging studies was explicitly regarded as the comparator. You, as a database user, should consider whether these are widely used health technologies in your own setting.

Validity of estimate of measure of effectiveness
The internal validity of the effectiveness results cannot be assured due to the retrospective nature of the study design. An attempt was made to decrease the biases by matching the patient groups with respect to age, sex, and tumour type. No power calculations were reported and it is not clear whether the sample size was appropriate for the study question. The degree to which the study sample was representative of the study population cannot be objectively assessed because insufficient information about the inclusion and exclusion criteria adopted in the study and patients’ baseline characteristics was presented in the paper.

Validity of estimate of measure of benefit
The estimate of benefit measure was directly derived from the effectiveness analysis. No justification was given for the choice of the benefit measure, and no alternatives, for example benefit measures such as life-years saved or quality-adjusted life-years saved, were discussed.

Validity of estimate of costs
Some useful details about the cost analysis were provided including the price year, and some details of the resource use and cost profiles. Statistical analyses were performed on resource use and cost data. However, the following characteristics may have undermined the validity of the cost results. The cost analysis was performed retrospectively, some important cost items were omitted from the cost analysis, the perspective adopted in the cost analysis was not specified, and charges were used instead of true costs. For the latter, the authors justified their decision. The effects of alternative procedures on indirect costs were not addressed. Sensitivity analysis was not performed to assess the robustness of the cost results.

**Other issues**

Given the inherent limitations of the study design, and lack of sensitivity analysis, the study results should be treated with some degree of caution. The issue of generalisability to other settings or countries was not addressed, but appropriate comparisons were made with other studies. The effectiveness analysis found similar health outcomes for both EUS and pre-EUS groups. From a methodological point of view the analysis was thus reduced to a cost-minimisation study requiring only a comparison of costs. However, the authors went on to report cost-effectiveness ratios. Given that the alternative diagnostic procedures were invasive, a cost-utility approach may have been a more appropriate framework to address the full range of effects and costs created by these procedures.

**Implications of the study**

The authors suggest that EUS should play a primary role in preoperative localisation of pancreatic neuroendocrine tumours. Similar analyses from other centres would supplement and perhaps support the authors' ability to generalise the results from a single study centre. The authors anticipated that accurate preoperative localisation should allow surgeons to perform more efficient exploration of the peripancreatic region, which might reduce perioperative morbidity.

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